This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. REGISTRATION NO. 93-R-0435 CUSTOMER NO. 9194

FORM APPROVED OMB NO. 0579-0036

## ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

HEADQUARTERS RESEARCH FACILITY (Name and Address, as registered with USDA, include Zip Code)

UNIVERSITY OF CALIFORNIA, LOS ANGELES 924 WESTWOOD BLVD., SUITE 1050 LOS ANGELES, CA 90024

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

(b)(2)High, (b)(7)(F)

A.  Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
4. Dogs			17		17
5. Cats		3			3
6. Guinea Pigs	237	430	21	737	1188
7. Hamsters					
8. Rabbits	8	209	389		598
9. Non-Human Primates		2	35		37
10. Sheep			1	14	15
11. Pigs	6		213	54	267
12. Other Farm Animals					
Chickens			40		40
13. Other Animals					
Chinchillas			12		12

- 1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.
- 2) Each principal investigator has considered alternatives to painful procedures.
- 3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the institutional Animal Care and Use Committee (IACUC). A summary of all the exceptions is attached to this annual report. In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.
- 4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL  (Chief Executive Officer or Legally Responsible Institutional official)  I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)						
SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	I NAME & TITLE OF CEO OF INSTITUTIONAL OFFICIAL (Type or Print)	DATE SIGNED				
(b)(6),(b)(7)(c)	(b)(6),(b)(7)(c)	11/20/2008				

APHIS FORM 7023 (AUG 91)

(Replaces VS FORM 18-23 (Oct 88), w

**PART 1 - HEADQUARTERS** 

1. Registration Number: 93-R-0435 / 9194

2/3. Species (common name) & Number of animals used in this study:

Guinea Pigs (737)

Aganesic n/a

- 4. Explain the procedure producing pain and/or distress.
  - 1) TB Studies (720 Guinea Pigs): (a) Vaccination for tuberculosis (TB) and (b) exposure to the TB organism (bacteria). The vaccine is given on one or more occasions to each guinea pig into the skin (intradermal), into the muscle (intramuscular), or under the skin (subcutaneous). At various times after vaccination, the guinea pigs are skin-tested to evaluate their immune response to the vaccine. This procedure is identical to the skin test normally performed on people (TB testing). Guinea pigs are later exposed (challenged) to an aerosol containing the TB organism. This exposure itself (inhalation) is not painful or distressful to the animals. One potentially painful event would be if a guinea pig developed a skin sore as a result of the vaccination or the skin test, as it occasionally happens in BCG-vaccinated people. During the past year, we have observed one such event, which the veterinarian treated successfully with topical analgesics (painkillers). Another instance that may potentially cause pain or distress is if the infection affects the membrane surrounding the lungs (pleura). Otherwise, pulmonary TB is considered to be a disease which is fairly free from pain. As the disease progresses, the infected guinea pigs lose their appetite and also lose weight. Animals are weighed daily to monitor progression of the disease, and they are immediately euthanized if they become moribund. 2) Leptospira Studies (17 Guinea Pigs): These studies involve infection of guinea pigs with Leptospira bacteria with the ultimate goal of developing a human vaccine for this disease. The leptospira bacteria are very difficult to grow in the Petri dish and, when they do, they dramatically change their biochemical characteristics. The only way to prevent these changes from occurring is by growing the bacteria inside guinea pigs. This is accomplished by giving the animals a low-volume injection of the leptospira organisms into the belly (intraperitoneal injection). The injection itself is not painful or distressful to the animals. However, guinea pigs have the potential to develop a rapid form of infection of the lungs (pulmonary form) which would then cause them to have breathing difficulty and pain. If this condition were to be detected, the guinea pig would be euthanized immediately by the veterinarian.
- 5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)
  - 1) TB Studies: The only medications that could possibly relieve any discomfort from TB would be anti-tuberculosis antibiotics. Treating the animals with antibiotics would defeat the purpose of the experiment, which is to assess the efficacy of a vaccine. If skin sores were noticed, a rare occurrence, the veterinarian would relieve the guinea pig's condition with topical analgesic drugs.

    2) Leptospira studies: Pain medications, such as morphine, can alter the animal's immune system (Opioids and the immune system, Palliat Med. 2006;20 Suppl 1:s9-15) and NSAIDs, such as Advil, have a direct effect on the inflammatory response, which is crucial for the establishment of this infection model. While the use of antibiotics would stop the infection, it would also kill the Leptospira bacteria we are attempting to grow for vaccine development.
- What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency. IIIa	OFR.
Approval Status: Approved/Disapproved By: Date:	
Disapproved Reason:	

CED.

1. Registration Number: 93-R-0435 / 9194

2/3. Species (common name) & Number of animals used in this study:

Sheep (14)

4. Explain the procedure producing pain and/or distress.

The objective of this study is to determine the mechanism by which low oxygen concentration (hypoxia) inhibits breathing in the fetus. These studies are relevant to sudden infant death syndrome (SIDS), sleep apnea and the general control of respiration. Lambs are gently held in a sling and their nose placed inside a standard anesthetic mask. After 5-10 minutes, the concentration of oxygen they breathe is lowered from 21% (normal oxygen concentration in air) to 7% for 15 minutes. This is immediately followed by a 10 minute recovery period. Though the reduction in oxygen tension is momentary, the lambs are expected to feel shortness of breath during this period, akin to what is experienced by mountain climbers at high altitudes.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

The lamb may not be anesthetized during this period because anesthetic drugs directly affect respiration, heart rate and blood pressure, which are the parameters concerned with this study. The potential distress of reducing the oxygen content of inhaled air from normal (21%) to lower concentrations in a conscious animal cannot be relieved by any sedative or tranquillizer either, since all of these drugs also affect the critical parameters of this research. The goals of the experiment could not be met if these drugs were to be administered. (Note: This study was discontinued in March 2008 and no further sheep are expected to be received at UCLA in the foreseeable future).

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency: n/a

CFR:

Approval Status: Approved/Disapproved By:

Disapproved Reason:

1. Registration Number: 93-R-0435 / 9194

2/3. Species (common name) & Number of animals used in this study:

Pigs (54)

4. Explain the procedure producing pain and/or distress.

Stage 1: While the pig is under continuous deep general anesthesia with gas (isoflurane), and after application of long-lasting local anesthesia with Marcaine to the groin area, small tubes (catheters) are carefully inserted into the superficial vein and into the artery of the groin. Thousands of human patients undergo an identical procedure daily for the placement of stent devices in the coronary arteries of the heart. The procedure in humans is done under mild sedation (Versed) and local anesthesia, and patients are typically instructed to take an over-the-counter painkiller (Tylenol or Advil) if they experience any discomfort after the procedure. Pigs cannot receive any medication after the procedures, as explained in the section below. Stage 2: With the pig still under general anesthesia, the blood circulation is stopped, which causes the blood flow to the brain to decrease. This procedure simulates what happens to human patients when they suffer a stroke subsequent to cardiac arrest. Stroke does not cause pain in humans and is not expected to be painful to animals either. Human patients may feel varying degrees of distress resulting from their awareness of being physically incapacitated, however. A comparable feeling would be impossible to assess in pigs. The cardiac arrest stage of the study, which would otherwise cause pain, is done under general anesthesia thereby ensuring that the pig does not feel any pain as a result.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

Pigs enrolled in this study may not receive any painkillers after the procedure because of interference with the body's response to the stroke and with the assessment of the animal's neurologic status. There are two general classes of painkillers available to us: Opiates (similar to Vicodine or morphine) or non-steroidal anti-inflammatory agents or NSAIDS (similar to Advil). Either one can potentially alter the normal inflammatory response to ischemia (lack of blood flow), as well as the subsequent white blood cell response involved in reperfusion injury (when blood flow returns to normal). Opiates, such as Vicodine, typically cause the animal (or the person) to be drowsy and somewhat incoordinated. That would make interpretation of the actual level of consciousness difficult to impossible. Nevertheless, in this project, the pig is monitored continuously around the clock for 24 hours following the stroke induction by trained laboratory staff, and then humanely euthanized. If a seizure were to occur (which has not happened to date), it would be controlled with diazepam (Valium). If the neurologic impairment were to be severe enough to affect assisted food and water consumption, the veterinarian would euthanize the animal.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency: n/a	CFR:	
Approval Status: Approved/Disapproved By: Date:	<i>/</i> :	
Disapproved Reason:		